

## Prevalence of Metabolic Syndrome and Related Characteristics in Obese Adolescents with and without Polycystic Ovary Syndrome

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**Context:** Adults with polycystic ovary syndrome (PCOS) may be at increased risk for metabolic syndrome (MBS) and related cardiovascular disease. It is not clear whether PCOS diagnosed in adolescence increases the risk of MBS in this age group.

**Objective:** The aim was to compare the prevalence and related characteristics of MBS in obese adolescents with and without PCOS.

**Design:** We conducted a cross-sectional study of overweight and obese PCOS adolescents and BMI matched controls.

**Patients and Participants:** A total of 74 subjects, 43 with PCOS and 31 controls, participated in the study.

**Interventions:** Each subject underwent a physical examination and laboratory evaluation for a diagnosis of MBS. Regional fat distribution was determined by computerized tomography scan in the PCOS adolescents.

**Main Outcome Measures:** We measured the prevalence of MBS and its components in adolescent subjects and controls.

**Results:** The PCOS group had larger ovarian volume and higher measures of total testosterone and free androgen index than controls, but there were no differences in waist circumference, fasting glucose, blood pressure, or lipids. PCOS adolescents demonstrated more glucose abnormalities and higher plasminogen activator inhibitor-1. By pediatric criteria, 53% of the PCOS and 55% of the control adolescents had MBS. By adult criteria, 26% of PCOS and 29% of controls met diagnostic criteria for MBS.

**Conclusions:** Obese adolescent women have a high prevalence of MBS, and PCOS does not add additional risk for MBS. There appears to be an association between MBS and visceral adiposity. PCOS is associated with increased incidence of glucose intolerance and increased plasminogen activator inhibitor-1. Our results reinforce the importance of obesity counseling in adolescents to recognize the possible risk of future cardiovascular disease in these young women. (*J Clin Endocrinol Metab* 93: 4780–4786, 2008)

**P**olycystic ovary syndrome (PCOS) is diagnosed by a combination of oligoovulation, clinical, and/or biochemical signs of hyperandrogenism, or ultrasound findings consistent with

polycystic ovaries (1). PCOS is associated with metabolic abnormalities, such as dyslipidemia, obesity, and glucose intolerance, which are also components of the metabolic syndrome

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Abbreviations: AUC, Area under the curve; BMI, body mass index; CRP, C-reactive protein; CT, computerized tomography; cv, coefficient(s) of variation; FAI, free androgen index; FG, Ferriman-Gallwey; HDL, high-density lipoprotein; IDF, International Diabetes Foundation; LDL, low-density lipoprotein; MBS, metabolic syndrome; PAI-1, plasminogen activator inhibitor-1; PCOS, polycystic ovary syndrome; VAT, visceral adipose tissue.

**TABLE 1.** Criteria for MBS in adults (11), adolescents (10), and IDF adolescents (13)

	Adult	Adolescent	IDF adolescent
Triglycerides	≥150 mg/dl or drug treatment for elevated triglycerides	≥110 mg/dl	≥1.7 mmol/liter
HDL cholesterol	<50 mg/dl or drug treatment for decreased HDL cholesterol	≤40 mg/dl	<1.03 mmol/liter
Fasting glucose	≥100 mg/dl or drug treatment for elevated glucose	≥110 mg/dl	≥5.6 mmol/liter or known type 2 diabetes
Waist circumference	≥88 cm (women)	≥90th percentile for age and sex	≥90th percentile (this element + 2 others required for IDF definition)
Systolic or diastolic blood pressure	≥135 mm Hg systolic or ≥85 mm Hg diastolic, or drug treatment for hypertension	≥90th percentile for age, sex, and height, or use of any antihypertensive drugs	>130 mm Hg systolic or ≥85 mm Hg diastolic

(MBS). The prevalence of MBS in adult premenopausal women with PCOS is approximately 40% (2). The prevalence of adolescent females with MBS in the United States is 12.4–44.2% (3). In one study using a national database (4), adolescents with PCOS were found to be at increased risk for MBS in comparison with controls; however, PCOS status could not be accurately ascertained in the control subjects. MBS prevalence in an adolescent PCOS cohort was found to be at least 3-fold higher when adjusted for body mass index (BMI) status (5).

Adults with MBS are at a greater risk of developing cardiovascular disease (6, 7). Cardiovascular risk is especially pronounced at younger ages in PCOS patients than in women without a history of PCOS (8, 9). Women with PCOS may be at even greater risk for cardiovascular disease because they are exposed to risk factors at a younger age.

The aims of this study are to establish the prevalence of MBS in obese, adolescent girls with and without PCOS and to examine the prevalence of related characteristics associated with MBS. We sought to determine whether PCOS increases the risk of MBS in obese adolescents. In addition, we analyzed serum markers of cardiovascular disease to determine whether they are elevated in obese adolescents with and without PCOS and whether such measures are independently associated with PCOS.

## Subjects and Methods

### Subjects and study design

We performed a cross-sectional study of overweight (BMI ≥ 25–29.9 kg/m<sup>2</sup>) and obese (BMI ≥ 30–46 kg/m<sup>2</sup>) postmenarcheal, nulliparous females, ages 12–18 yr. A total of 74 subjects were enrolled, 43 with diagnosis of PCOS and 31 BMI-matched controls. PCOS was defined by the 1990 National Institutes of Health criteria. PCOS subjects had evidence of menstrual irregularity (fewer than eight cycles per year) and clinical or biochemical evidence of hyperandrogenism. Although a transabdominal ultrasound was performed on all subjects, it was not used as a criterion for the diagnosis of PCOS. Subjects were recruited by direct advertisement in the community or by referral by pediatricians, family doctors, or local OB/GYN physicians.

Overweight or obese adolescents with regular menstrual cycles (<45-d intervals) and no signs of androgen excess served as controls. All subjects were studied at the University of Rochester Medical Center (URMC) in the Division of Reproductive Endocrinology. Metabolic and hormonal studies were performed at the URMC General Clinical Re-

search Center. The study was approved by the Research Subjects Review Board at the University of Rochester, and all subjects provided signed consent if they were 18 yr of age or older or gave assent with signed consent by parent or legal guardian.

Adolescents were included if they fulfilled the age and weight criteria stated above. Exclusion criteria were pregnancy, diagnosis of diabetes mellitus, other endocrinopathy (congenital adrenal hyperplasia, thyroid dysfunction, and hyperprolactinemia), the use of combined oral contraceptive or other medications known to affect gonadal or adrenal function or carbohydrate or lipid metabolism within the 2 months preceding enrollment in the study, tobacco or alcohol use, or a history of ovarian surgery. We defined MBS as reported by Cook (10) (Table 1) using pediatric criteria. We also used the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) definition of MBS for adults and the International Diabetes Foundation (IDF) definition for MBS in adolescents (11–14) (Table 1). For all definitions, the presence of three or more criteria resulted in the diagnosis of MBS, with the IDF definition requiring an increased waist circumference in addition to two other features.

### Study protocol

All subjects who were enrolled in the study had a medical history and underwent physical examination, including determination of Ferriman-Gallwey (FG) scoring of hirsutism. Weight was measured in kilograms, and height was measured to the nearest 0.5 cm. BMI was calculated. Blood pressure was measured in the supine position and averaged over three measurements. Waist circumference was measured in centimeters via tape measure at the widest point between the lower border of the right costal margin and the top of the iliac crest. With a semi-full bladder, the subjects then underwent a transabdominal ultrasound examination to visualize the ovaries and uterus and to calculate ovarian volume.

At a separate visit, eligible subjects were studied at the URMC General Clinical Research Center. Subjects with regular menses were studied in the early follicular phase of the menstrual cycle. Those with oligomenorrhea were studied without regard to the timing of menstrual bleeding. Urine pregnancy tests excluded pregnancy. Subjects were asked to stay on a weight-maintaining diet consisting of at least 500 calories of complex carbohydrates a day for 3 d before the visit. Subjects arrived in the fasting state, confirmed by reporting the last time they ate or drank anything other than water, and blood samples were obtained and analyzed for total testosterone, SHBG, lipid profile, C-reactive protein (CRP), adiponectin, and plasminogen activator inhibitor-1 (PAI-1). An oral glucose tolerance test was then administered with 75 g of oral glucose given at time 0. Samples were then obtained from an indwelling catheter at 30, 60, and 120 min. Glucose and insulin levels were determined at each of the four points. Dual-energy x-ray absorptiometry (DEXA-QDR 4500 Elite; Hologic, Bedford, MA) was performed to estimate body fat.

Visceral and sc adipose tissues were calculated for each PCOS subject using a single image computerized tomography (CT) scan at the L4-L5 vertebral interspace. Tomovision SliceOmatic CT software (Tomovision, Montreal, Canada) was used to assign sc adipose tissue and visceral adipose tissue (VAT) based upon assigned tissue density.

## Assays

After sample collection, sera was extracted and stored at  $-80^{\circ}\text{C}$ . Both CRP and SHBG were measured by the Immulite system (Diagnostic Products Corp., Los Angeles, CA); interassay coefficients of variation (cv) were 6.7 and 8.7%, respectively. Insulin was measured by  $^{125}\text{I}$  immunoradiometric assay (Linco Research, Inc., St. Charles, MO); inter- and intra- assay cv were 4.7 and 3.3%. Testosterone was measured by RIA (Diagnostic Systems Laboratories, Webster, TX) (cv, 8.5%). PAI-1 was measured by two-site ELISA (inter- and intra- assay cv 3.5 and 10%; normal range, 5–66 ng/ml). Glucose was measured by YSI select analyzer (YSI Inc., Yellow Springs, OH). Total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were measured by dry slide enzymatic colorimetric assay (Vitros Products, Ortho-Clinical Diagnostics, Rochester, NY). HDL was separated by precipitation of low-density lipoprotein (LDL) and very low-density lipoprotein using dextran sulfate and magnesium chloride and was removed by centrifugation. LDL was assayed by enzymatic cholesterol assay (Sigma Diagnostics, St. Louis, MO) after precipitation of VLDL and HDL. Adiponectin was measured using an RIA procedure (Linco Research, Inc.) (cv, 8.0%). The free androgen index (FAI) was calculated by the equation:  $\text{FAI} = (\text{testosterone}/\text{SHBG}) \times 100$ . The area under the curve (AUC) for glucose and insulin during the oral glucose tolerance test were calculated using the trapezoid rule.

## Statistical analysis

Results are reported as means (SD) unless otherwise stated. All analyses were performed using SAS (version 9.1; SAS Institute Inc., Cary, NC). Group differences were analyzed using *t*-tests for continuous variables and Fisher's exact test for categorical values. A one-way ANOVA was used to compare the adolescents by their number of MBS components. Two-tailed *P* values  $< 0.05$  were considered significant.

## Results

### Demographics and anthropometrics

All 43 subjects with diagnosis of PCOS had menstrual abnormalities and clinical evidence of androgen excess, with either elevated serum androgens or clinical hirsutism with an elevated FG score of at least 6 (15). A total of 90% of the subjects with PCOS had an elevated total testosterone or FAI. Hirsutism was noted in 87.5% of the PCOS adolescents, with the FG score ranging between 5 and 22. Mean menstrual cycle length in 39 PCOS subjects was 92.7 d, and four additional subjects had amenorrhea of at least 1 yr after initially irregular cycles. Thirty-one adolescent females served as BMI-matched controls. The mean menstrual cycle length in these subjects was 26.9 d. Table 2 demonstrates the ethnic and racial characteristics of the study groups. There were no significant differences in weight, BMI, or percent body fat, although the control subjects were slightly younger.

### Endocrine features

As would be expected with the diagnosis of PCOS, the study group had significantly higher measures of total testosterone and FAI. The mean FG score in PCOS subjects was  $9.6 \pm 3.9$  vs.  $3.4 \pm$

**TABLE 2.** Demographics and anthropometric data

Characteristic	Controls (n = 31)	PCOS (n = 43)	P value
Age (yr)	14.8 (1.8)	15.6 (1.5)	0.0394
Race/ethnicity, n (%)			0.098
Asian, non-Hispanic	2 (6)	0 (0)	
Black, non-Hispanic	9 (29)	7 (16)	
Hispanic	4 (13)	4 (9)	
White, non-Hispanic	13 (41)	30 (69)	
Other, non-Hispanic	3 (10)	2 (5)	
Weight (kg)	92.8 (27.0)	98.7 (3.1)	0.1757
Height (cm)	165.2 (5.7)	164.1 (5.8)	0.4457
BMI ( $\text{kg}/\text{m}^2$ )	34.0 (5.2)	36.6 (6.9)	0.0860
Z-score	2.18 (0.39)	2.18 (0.38)	0.4814
Percentile	97.5 (2.8)	97.7 (2.7)	0.6105
% Body fat	41.93 (4.7)	42.97 (4.4)	0.337

Data represent mean (SD), unless indicated otherwise.

1.7 in controls ( $P < 0.0001$ ). Ovarian volume was greater in the PCOS subjects (Table 3). Ultrasound in this study was performed by the transabdominal route. The significant abdominal adiposity present in the subjects and the need for transabdominal scanning made Rotterdam morphologic ultrasound criteria for polycystic ovaries difficult to accurately assess, so morphologic data were not included. There was no significant difference in adiponectin ( $8.6 \pm 2.2$  mg/liter in controls vs.  $9.7 \pm 4.4$  mg/liter in PCOS subjects;  $P = 0.2$ ).

### Cardiovascular risk variables

There were no significant differences between the PCOS adolescents and the control adolescents in waist circumference, fasting glucose or insulin, blood pressure, components of the cholesterol panel, or CRP. AUC glucose and AUC insulin were significantly greater in the PCOS subjects compared with controls (Table 4). The incidence of impaired fasting glycemia or impaired glucose tolerance, as defined by fasting glucose of at least 100 mg/dl (four subjects) or 2-h glucose of at least 140 mg/dl (six subjects), was 25% in PCOS. The control group had significantly fewer subjects with abnormal glucose tolerance, with a single subject with an elevated 2-h glucose and none with impaired fasting glycemia ( $P = 0.01$ ).

Mean PAI-1 levels were significantly higher in PCOS adolescents compared with controls ( $52.4$  vs.  $37.1$  ng/ml;  $P = 0.034$ ). PAI-1 was correlated with percentage body fat ( $r = 0.29$ ;  $P = 0.01$ ), FAI ( $r = 0.30$ ;  $P = 0.001$ ), BMI ( $r = 0.42$ ;  $P = 0.002$ ), and waist circumference ( $r = 0.45$ ;  $P < 0.0001$ ).

**TABLE 3.** Endocrine characteristics

Characteristic	Controls (n = 31)	PCOS (n = 43)	P value
Total testosterone (ng/dl)	41.9 (16.2)	60.1 (24.9)	0.001
FAI	8.5 (5.1)	16.4 (11.9)	0.001
SHBG (nmol/liter)	21.2 (10.0)	18.4 (13.1)	0.312
Ovarian volume ( $\text{cm}^3$ )	5.0 (1.7)	7.8 (3.0)	$< 0.0001$

Data represent mean (SD).

**TABLE 4.** Cardiovascular risk factor values by group

Factor	Controls (n = 31)	PCOS (n = 43)	P value
Central obesity			
Waist circumference (cm)	105 (10)	108 (15)	0.3146
Insulin resistance			
Fasting glucose (mg/dl)	87 (5)	88 (17)	0.8020
Fasting insulin (mIU/ml) <sup>a</sup>	20.7 (1.6)	22.4 (1.7)	0.5014
2-h glucose (mg/dl)	111.5 (15.8)	122.0 (29.6)	0.0761
AUC glucose	17,324 (2,114)	19,260 (2,760)	0.0018
AUC insulin	17,514 (9,553)	26,228 (18,403)	0.019
CRP (mg/liter)	3.5 (3.1)	5.3 (4.7)	0.3658
Hypertension (mm Hg)			
Systolic blood pressure	118 (13)	114 (13)	0.2852
Diastolic blood pressure	64 (9)	67 (9)	0.1686
Dyslipidemia (mg/dl)			
Total cholesterol	154 (22)	164 (28)	0.1027
LDL cholesterol	107 (22)	114 (.24)	0.2083
HDL cholesterol	40 (6.5)	39 (8.2)	0.4424
Triglycerides <sup>a</sup>	90 (1.4)	90 (1.5)	0.9856
Used tobacco (%)	0	10	0.132
PAI-1 (ng/ml)	37.1 (22.9)	52.4 (34.1)	0.034

Data represent mean (sd) unless indicated otherwise.

<sup>a</sup> Geometric mean.

## MBS

With respect to diagnosis of MBS within the range of BMI in the cohort, there was an association between the features of MBS and increasing BMI ( $r = 0.23$ ;  $P = 0.05$ ). Using the pediatric criteria, 55% of the control group and 53% of the PCOS group fit the criteria for MBS (Table 5). The IDF has proposed a definition of MBS that has recently been adapted for adolescents and is detailed in Table 1 (13, 14). The adolescent IDF criteria require a waist circumference of at least the 90th percentile associated with two additional elements. Using these criteria, 19% of controls and 26% of cases ( $P = 0.586$ ) would meet the diagnosis of

**TABLE 5.** Prevalence of metabolic factors by group

Factor	Control (n = 31)	PCOS (n = 43)	P value
Adult ATP III criteria			
Adult waist circumference $\geq 88$ cm	97	93	0.635 <sup>a</sup>
HDL $\leq 50$ mg/dl	90	93	0.690 <sup>a</sup>
Adult blood pressure $\geq 130/85$ mm Hg	20	14	0.534
Triglycerides $\geq 150$ mg/dl	13	9	0.713 <sup>a</sup>
Glucose $\geq 100$ mg/dl	0	9	0.135 <sup>a</sup>
Pediatric ATP III criteria			
Pediatric waist circumference $\geq 90^{\text{th}}$ percentile	87	88	0.999 <sup>a</sup>
HDL $\leq 40$ mg/dl	55	70	0.188
Pediatric blood pressure $\geq 90^{\text{th}}$ percentile	45	27	0.125
Triglycerides $\geq 110$ (mg/dl)	26	37	0.301 <sup>a</sup>
Glucose $\geq 100$ (mg/dl)	0	9	0.135 <sup>a</sup>
Overall Rates of MBS			
Pediatric, $\geq 3$ above factors	55	53	0.908
Pediatric IDF definition, $\geq 3$ above factors	19	26	0.586
Adult, $\geq 3$ above factors	29	26	0.742

Data are expressed as percentage.

<sup>a</sup> Used Fisher's exact test.

**TABLE 6.** VAT levels compared to number of positive components in MBS

VAT (cm <sup>2</sup> )	No. of MBS factors			P value
	0–1	2	3+	
Mean (sd)	68 (29)	91 (36)	128 (31)	0.0049
n	5	25	10	

MBS. Using the adult criteria, 29% of the controls and 26% of the PCOS subjects met MBS criteria. Furthermore, there were no significant differences in any specific factors of MBS between the two groups. FAI was not significantly different between those with and without MBS in either the PCOS group (16.4 *vs.* 14.4;  $P = 0.5533$ ) or the controls (7.9 *vs.* 8.9;  $P = 0.5908$ ).

## VAT

Within the PCOS cohort, VAT levels were significantly higher in the MBS group ( $P = 0.0027$ ). When the numbers of MBS factors are compared, those with three or more factors have significantly greater VAT (Table 6). Insulin ( $r = 0.5069$ ;  $P = 0.0010$ ) and homeostasis model assessment ( $r = 0.5183$ ;  $P = 0.0007$ ) were significantly correlated with higher VAT. Neither total testosterone nor FAI was significantly correlated with VAT ( $r = -0.2882$ ,  $P = 0.0713$ ; and  $r = -0.2715$ ,  $P = 0.0902$ , respectively). Using the adult components for MBS, except for waist circumference, fasting glucose and triglycerides were significantly associated with higher levels of VAT (Table 7).

## Discussion

Body weight plays a role in the endocrine status of adolescent women. The prevalence and degree of obesity has rapidly increased over the last several decades. The Center for Health Statistics of the Centers for Disease Control has been collecting data from the National Health and Nutrition Examination Survey (NHANES) since 1963. In 1999–2000, the prevalence of overweight was 14.8% among a representative sample of American females aged 2–19 yr, and in 2003–2004, prevalence was 16.4% (16). In comparison, approximately 5% of adolescents were overweight in the 1960s to 1970s. Furthermore, the prevalence

**TABLE 7.** Mean VAT by each factor of MBS

Factor	Mean VAT (cm <sup>2</sup> )		P value
	Abnormal	Normal	
Blood pressure			0.2938
Mean (sd)	113 (27)	94 (40)	
n	6	34	
HDL			0.3685
Mean (sd)	99 (39)	77 (37)	
(<40 mg/dl) n	37	3	
Triglycerides			0.0264
Mean (sd)	144 (19)	93 (38)	
( $\geq 150$ mg/dl) n	3	37	
Glucose			0.0009
Mean (sd)	165 (17)	92 (35)	
( $\geq 100$ mg/dl) n	3	37	

of obesity in PCOS is currently about 70%, 20% higher than 15 yr ago (17).

In particular, waist circumference, a measure of abdominal obesity, has increased since 1988, with the greatest increases in older adolescent females (18). In PCOS, a central fat distribution is more common, with visceral fat predominating over peripheral fat (19). Obesity, as measured overall by BMI, influences the prevalence of MBS. Our study suggests that, when matched for obesity, a diagnosis of PCOS is not associated with increased risk of MBS using either pediatric or adult criteria.

All of the adolescents in the current study were overweight or obese, and those with MBS had greater VAT in the PCOS subset. Specifically, the VAT increased with increasing numbers of MBS characteristics. We found that VAT was correlated with insulin resistance, consistent with previous reports (20). Nonobese PCOS women are found to have greater abdominal adiposity, and this is associated with greater inflammatory profiles (21, 22). Yildirim *et al.* (23) compared nonobese PCOS women with controls and found that women with PCOS had significantly greater preperitoneal and visceral fat, and that increased visceral fat was associated with high fasting insulin and triglyceride levels. A recent study demonstrated no difference in abdominal fat distribution between those with obesity with and without PCOS (24). However, the average BMI was only 28 kg/m<sup>2</sup>, classifying these women as overweight, not obese, and the groups were not matched for age, which may influence abdominal adiposity. Because our study included only overweight or obese adolescent women, we are unable to compare the rates of MBS in a normal weight population of adolescent women with and without PCOS. Although the true prevalence of obesity in adolescent women with PCOS is not known, given the dramatic rise in obesity in the adolescent population overall, it likely mirrors that in young adult women. This makes assessments in a weight-matched population of overweight or obese adolescents relevant to the clinical management questions.

Traditional cardiovascular risk factors may be increased in obesity and in PCOS and are associated with increased inflammation, oxidative stress, and coagulation abnormalities, with subsequent endothelial and myocardial dysfunction and arterial stiffness (25). Women with PCOS have demonstrated impairment of the glucose tolerance, lipid profiles, blood pressure (26, 27), and increased left ventricular mass with diastolic dysfunction, which may lead to cardiovascular disease (28). Even young women (less than 45 yr old) with PCOS show subclinical coronary atherosclerosis as detected by the presence of coronary artery calcium (29). Insulin resistance is a key component of PCOS (30). In perimenopausal women, non-insulin-dependent diabetes mellitus and cardiovascular disease were more likely in women who had a history of PCOS (31). Despite the lack of difference in MBS between groups, our study demonstrates a significantly increased risk of impaired fasting glycemia or impaired glucose tolerance in adolescents with PCOS compared with weight-matched controls, as well as increased serum PAI-1. This supports a potentially increased cardiovascular risk in these individuals compared with weight-matched adolescents without PCOS, regardless of MBS diagnosis.

One half of obese adolescents in our study; regardless of PCOS status, have MBS according to the pediatric definition, and 19–29% fit the adult or IDF adolescent criteria. Using the same criteria as in our study for the pediatric definition of MBS, Coviello *et al.* (4) found a prevalence of 38–40% of MBS in their PCOS adolescents, which was associated with increasing BMI. Furthermore, they report increased rates of MBS in their PCOS subjects compared with a national dataset, although they were not matched on BMI. They also found increased blood pressure in the PCOS subjects. They demonstrated a relationship between hyperandrogenemia and MBS in the PCOS subjects. The relationship between elevated androgens and hypertension in young PCOS women has also been demonstrated by Chen *et al.* (32), even after controlling for age and BMI. The current study and another (33) did not find that MBS was associated with androgen concentration within PCOS or control subjects; both of these studies were performed in overweight or obese populations. Our study collected control women directly from a similar population of young women who were of similar weight with documented endocrine and menstrual history. The prior study of MBS in adolescent women (4) was unable to truly assess the endocrine characteristics of the control population because neither menstrual data nor androgens were recorded in the database for controls. It is possible that the impact of obesity is a more significant contributor to the prevalence of MBS than endocrine status.

Our data show that obesity is strongly associated with MBS in adolescent women, whether or not they have PCOS. This is particularly notable in the presence of increased VAT. Adolescents with PCOS demonstrate abnormal insulin secretion and action (34). There may be an associated pathophysiological link with obesity, particularly visceral adiposity, and related adipose tissue factors, coagulation abnormalities, or insulin resistance (2) that may independently increase cardiovascular risk.

Another marker of cardiovascular risk is PAI-1. PAI-1 is a glycoprotein that may influence vascular function by inhibiting fibrinolysis. Our PCOS subjects had significantly higher levels of PAI-1 than the obese control adolescents, and this correlated with androgen levels. This is consistent with previous findings in which PAI-1 activity was increased in obese, adult women (35) and in young, lean women with PCOS (36). The hyperglycemia and hyperinsulinemia characteristic of PCOS can also be related to increased PAI-1 activity (37).

Our study was limited by its small sample size. Visceral adiposity was also not measured in the control subjects to validate the relationship of visceral adiposity and MBS outside of the PCOS subset. A potential limitation of the study is the use of the RIA for testosterone. We recognize that the reliability of immunoassays for testosterone is reduced in the lower ranges found in adolescent women, and this may make it difficult to categorize subjects properly by androgen level only. However, this is unlikely to alter the main conclusions. First, we used the NIH classification for PCOS, incorporating clinical as well as biochemical measures. Additionally, in this generally obese population, measurement of androgen concentration across both groups, separately and without respect to diagnosis of PCOS, was not associated with diagnosis of MBS.

The criteria for MBS in adolescents are not yet validated for outcome measures related to cardiovascular disease. When applying the adult definition for MBS, other studies report that as many as one in four obese teens meet these criteria (12). Although the data are limited, there are reports suggesting that adolescents identified with MBS using these criteria will go on to have increased risk for diabetes mellitus or increased risk for coronary artery disease in adulthood (38, 39).

Our data indicate that, in obese adolescents, obesity is a stronger predictor of MBS than is PCOS status. Our data further suggest that the effect of obesity is mainly accounted for by visceral adiposity. This finding emphasizes the importance of obesity counseling in obese adolescent women to reduce the risks associated with MBS. Further studies are needed to determine relationships between MBS, PCOS, and androgens, particularly in the nonobese adolescent cohort.

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